REMARKS/ARGUMENTS

Claims 1, 3, 6, 7, 10-12, 15-20, 23, and 26-35 are pending in the subject application. Of these, claim 6 had been withdrawn from consideration, but the Examiner has indicated in the present Office Action that it is being examined, so the status in the above claims listing has been amended appropriately. Claims 1 and 26 have been amended to correct a typographical error, replacing "of" with "or". Claims 1, 6, 7, 15, 23, 26, and 33 have been amended to remove the word "modified', in order to clarify the meaning of the claims. Claims 1, 26 and 33 are amended to clarify what is meant by Ret receptor kinase. Support for the claim amendments can be found in the specification as filed, at for example paragraphs 0026-0032 in the specification as filed. Applicants have made these amendments without relinquishing their right to pursue patent protection for unclaimed subject matter in a subsequent application.

In the Office Action mailed December 28, 2007 the Examiner rejected Claims 1-4, 7-8, 10-12, 15-20, 23, and 26-37 under U.S.C. 102(b), as being anticipated by Rizzo et al. (1996) J. Biol. Chem. 271(46):29497-29501. Since this rejection is not repeated in the present Office Action applicants assume that it has been overcome by arguments and /or amendments in the response filed 5/23/08.

I. Rejections Under 35 USC 112, second paragraph:

In the Office Action mailed August 20, 2009 the Examiner rejected Claims 1, 3, 6-7, 10-12, 15-20, 23, and 26-35 under U.S.C. 112, second paragraph. The Examiner stated that because "Ret receptor kinase" and other receptors disclosed in the instant application are identified by name, and not by structure, that the metes and bounds of the terms used are allegedly not clear.

On page 4 of the Office Action the Examiner also made the following statements:

> "Furthermore, the names of receptors change over time or are named differently by different inventors or scientists thus it becomes a relative term."

> "For example, when is a Ret receptor kinase which can have unlimited substitution different from any other kinase receptor? For example the EGFR is a kinase receptor and appears to meet the limitations of the Ret receptor kinase as claimed without structural limitation."
>
> "Furthermore, if the Ret kinase receptor can have unlimited changes then how is one skilled in the art able to determine what is the specific amino acid sequence number that should be substituted."
>
> "Furthermore, if the Ret receptor kinase can have unlimited mutations then when is Ret kinase receptor a rat receptor versus the human receptor or any other species."

In response, as indicated previously, applicants respectfully disagree that the term "human Ret receptor kinase" is ambiguous in the context in which it is used in the instant specification. Only one human receptor tyrosine kinase was termed "Ret" at the time of filing of the instant application. This is presently still true. Thus the statement by the Examiner that the names of receptors change over time or are named differently by different inventors is not relevant here. No other receptor kinase has been named "Ret", and thus there is no ambiguity. With respect, the Examiner has presented no evidence to dispute this fact (e.g. multiple "Ret" kinase genes with different structures), and thus the Examiner's concern about "Ret" being a relative term is merely hypothetical in this instance.

The Examiner is correct that there are many different types of mutations of Ret kinase species in the literature. However, applicants respectfully submit that this fact is not relevant to the currently pending claims. The Ret portion of the hybrid receptors of the instant claims is limited to being substituted at one or more of only six specific cysteine residues, i.e. Cys 609, Cys611, Cys618, Cys620, Cys630 and Cys634. No other modifications are present versus the native Ret molecule. To help clarify this applicants have amended claims 1, 6, 7, 15, 23, 26, and 33 to remove the word "modified', in case this is being interpreted as including other modifications. In addition, claims 1, 26, and 33 have been amended to include the phrase "wherein human Ret receptor kinase has a protein sequence as published in the genetic sequence database GENBANK®" The reference to human Ret kinase protein sequences in Genbank® unambiguously identifies that what is meant in the claims by human Ret kinase is the native sequence, with the specific stated cysteine substitutions. Although there are two human Ret kinase transcript variants in

Genbank®, their protein sequences are identical in their extracellular domains, and thus no anbiguity is presented. Furthermore, the position and numbering of the juxtamembrane cysteine residues in the Genbank® protein sequences is identical to that used in the instant specification and claims, i.e. Cys 609, Cys611, Cys618, Cys620, Cys630 and Cys634, so it is clear what modifications of the human Ret kinase are intended in the instant claims (see Exhibits A and B for copies of the database entries for human Ret kinase). It should also be noted that these sequences were publicly available in Genbank® prior to the filing date of the instant application. Support for this amendment can be found in the instant application at paragraph 0032, where it is indicated that the sequence for the Ret receptor can be found in Genbank®. It should also be noted that in paragraph 0032 the Ret receptor is also designated as the GDNF receptor, which provides additional support for the identity of Ret.

In several of the Examiner's statements he indicates that the Ret receptor kinase of the claims can have unlimited substitution, changes or mutations. Applicants respectfully submit that this was clearly not true even prior to the instant claim amendments, and even less true now. In the instant claims the Ret kinase section is described as follows:

".....extracellular domain of human Ret receptor kinase, containing one or more amino acid residue substitutions.....wherein the one or more amino acid substitutions occur at residues selected from Cys 609, Cys611, Cys618, Cys620, Cys630 or Cys634..... wherein human Ret receptor kinase has a protein sequence as published in the genetic sequence database GENBANK®."

Thus, even without the instant amendment, applicants respectfully submit that it is clear that the claims do not describe unlimited substitution, changes or mutations of human Ret receptor kinase. The modifications are restricted to six cysteine residues. Applicants realize that when the Examiner is interpreting claims, the claims must be "given their broadest reasonable interpretation consistent with the specification." (MPEP 2111). However, applicants respectfully submit that to give the claims such a broad interpretation that "Ret receptor kinase" can be "EGFR receptor kinase" is not "reasonable", is not consistant with the language of the claims, and is not an interpretation consistant with the teachings of the specification.

With respect to other receptor kinases recited in the claims, the only one present in the instant claims is human tie2 kinase in claim 3. In paragraph 0032 of the specification it is indicated that the sequence for human tie2 receptor is publicly available in Genbank®. Furthermore, it is also indicated here that the sequence for TEK receptor, which is the official name for the human tie2 receptor (see Exhibit C for database entry), is publicly available in Genbank®. It should also be noted that this sequence for human tie2 kinase was publicly available in Genbank® prior to the filing date of the instant application. It also indicates in this paragraph that this is the receptor for angiopoietin, further clarifying what receptor is being identified. Thus applicants respectfully submit that there is no ambiguity as to the nature of human tie2 kinase in claim 3, and thus as to the identity of the kinase domain to which the claim refers.

Accordingly, in view of the above arguments and amendments, applicants respectfully submit that one of skill in the art would have no problems in understanding what is meant by the receptor kinases described in the instant claims, and thus that all rejections under 35 USC 112 have been overcome and request their withdrawal.

II. Conclusion

In view of the arguments and amendments set forth above, applicants respectfully request that the Examiner reconsider and withdraw the grounds for rejection, and that a timely Notice of Allowance be issued in this case.

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Respectfully submitted,
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